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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,876	06/08/2006	Roy Larsen	50147/010001	9168

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
02/02/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,876	LARSEN ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/5/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/10 has been entered.

Status of Claims and Previous Rejections

2. Claims 14-17 are pending in the application.

3. The rejection of claims 14-17 under 35 U.S.C. 103(a) as being unpatentable over Larsen et al. (US 2001/0008625A1) in view of Larsen et al. (WO02/05859A2) is withdrawn.

New Ground of Rejection

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacques et al. (*J. Alloys Compds.* **1994**, *213/214*, 286-289; abstract) in view of Deal et

al. (*J. Med. Chem.* **1999**, *42*, 2988-2992) and Larsen et al. (US 2001/0008625A1) and in further view of Ma et al. (US 2003/0086868A1).

6. Jacques et al. (*J. Alloys Compds.* **1994**, *213/214*, 286-289; abstract) discloses thorium (IV) complexes of two polyaza polycarboxylic macrocycles, DOTA and HEHA (abstract).

7. Jacques et al. does not disclose ^{227Th}, a targeting moiety with bioaffinity or the method for forming a ^{227}Th-DOTA complex comprising a targeting moiety with bioaffinity.

8. Deal et al. (*J. Med. Chem.* **1999**, *42*, 2988-2992) discloses ^{225}Ac-complexes, such as HEHA, DOTA, PEPA used for radioimmunotherapy. The ^{225}Ac-complexes show exceptional in vivo stability, reduced toxicity and permitted substantial accumulation of the radionuclide to the liver, as a result of the chelation of the ^{225}Ac to the chelating agents (abstract; p2988, Results and Discussion; p2990; p2991, left column). Limited studies which thorium (IV) and HEHA suggested a thermodynamically and kinetically stable complex was formed for this article (p2991, first paragraph).

9. Larsen et al. (US 2001/0008625A1) discloses a receptor binding conjugates comprising a radionuclide (i.e. ^{227}Th, ^{225}Ac or ^{223}Ra, etc.), an antibody, and a folate (derivative), such as oestrogen or testosterone for affinity to breast or prostate cancer. The conjugates of the disclosure are specifically directed to the soft tissue site containing the receptor (p1, [0001]; p2, [0016],[0020],[0025]; claims 19 and 20).

10. Ma et al. (US 2003/0086868A1) discloses ^{225}Ac conjugates comprising a functionalized chelant wherein the ^{225}Ac complex is covalently attached to a biological

molecule (e.g. hapten, antigen, etc.) to provide for tumor specificity in the treatment of cancer (p1, [0012-0013]; p2, [0014-0032], [0041-0044]). The conjugates of the disclosure may be administered as a component of a pharmaceutically acceptable formulation, such as in association with a carrier, excipient or vehicle (p3, [0047-0049]).

11. The ^{225}Ac conjugates of the disclosure can be prepared by first forming the complex, such as with heating (i.e. 50°C) and then binding the biological molecule (p5, [0097]; example 1).

12. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the thorium (IV) of Jacques et al. for the ^{227}Th of Larsen et al. as Deal et al. teaches that ^{225}Ac and thorium (IV) successfully form complexes with HEHA, DOTA for radioimmunotherapy and Larsen et al. teaches that ^{227}Th, ^{225}Ac are analogously used for treating cancer. Thus, the substitution of thorium (IV) for ^{227}Th predictably provides for complexes that are useful for radioimmunotherapy as evidence by the equivalence of ^{225}Ac-DOTA complexes and those comprising ^{227}Th. Further, Jacques et al. also teaches that thorium can be predictably conjugated to the DOTA chelating ligand.

13. At the time of the invention it would have been obvious to one ordinarily skilled in the art to covalently bind a biological molecule, such as that of Ma et al. to the ^{227}Th - DOTA complexes of the combined disclosures and incorporate them into a pharmaceutical composition, to provide the advantage of tumor specificity in the treatment of cancer as taught by Ma et al.

14. At the time of the invention it would have been obvious to one ordinarily skilled in the art to prepare the ^{227}Th -DOTA complexes of the combined disclosures via the method of Ma et al. that teaches of standard radionuclide conjugation reaction conditions for chelation to the chelating agent, DOTA.

Response to Arguments

15. Applicant asserts that Larsen '625 describes receptor binding conjugates which are directed to or against tumors expressing a folate binding protein. These conjugates include an antibody, a radionuclide and a folate, where the radionuclide is bound through the use of a bifunctional chelator with coupling reactivity toward certain groups on the proteins.

16. The reference of Larsen '625 was not explicitly used to teach of the receptor binding conjugates but was used to teach that the ^{225}Ac, ^{227}Th radionuclides are analogously used for the treatment of cancer and the substitution of ^{225}Ac for ^{227}Th is predictable.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618